

ORIGINAL



Predictive factors of successful renal replacement therapy weaning

Deciding On patients Orientations after Renal replacement therapy Stopping (The DOORS study)

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Abstract

Introduction: Renal replacement therapy (RRT) is a life-saving intervention in severe acute kidney injury (AKI). After a clinician-initiated discontinuation, the likelihood of sustained liberation remains uncertain. We aimed to identify predictors of successful RRT weaning and to develop a pragmatic bedside tool (the UNDERScore) to support post-discontinuation management.

Methods: This post-hoc analysis of two multicenter randomized trials (AKIKI and AKIKI2) included ICU patients with KDIGO stage 3 AKI managed with a conservative initiation approach. Patients were eligible if they underwent an RRT weaning attempt, defined as discontinuation for ≥ 3 consecutive days. The primary outcome was successful weaning, i.e., no RRT resumption within seven days. Independent predictors were identified using multivariable logistic regression, and the resulting model (UNDERScore) was externally validated in an independent Swiss ICU cohort.

Results: Among 554 patients who received RRT, 180 underwent a weaning attempt and 101 (56%) were successfully weaned. Six predictors were retained to construct the UNDERScore: RRT duration before the attempt, septic shock on admission, baseline serum creatinine, and three clinical variables assessed after the weaning attempt (use of vaso-pressors, invasive mechanical ventilation, and urine output). The score showed strong discrimination in the derivation cohort (AUC 0.86, 95% CI 0.80–0.91). In the external Swiss cohort ($n=415$), 338 patients (81%) were successfully weaned, with fair performance across a broader case mix (AUC 0.73, 95% CI 0.66–0.80).

Conclusion: The UNDERScore, derived from a homogeneous conservative RRT initiation cohort and validated in a diverse ICU population, provides a bedside tool to estimate the probability of sustained RRT discontinuation after an initial clinician-initiated stop.

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A list of the DOORS investigators is provided in the Electronic Supplementary Materials.



Graphic abstract:

PREDICTIVE FACTORS OF SUCCESSFUL RRT WEANING Deciding On patients Orientations after Renal replacement therapy Stopping (The DOORS study)

Clinical Question

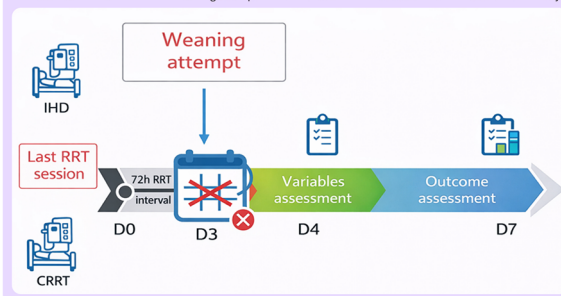
Can we predict sustained RRT discontinuation after a clinician-initiated stop in ICU patients with severe AKI?

Key Findings:

UNDERSCORE: A simple bedside score to guide catheter removal vs maintaining access after RRT discontinuation.

Study Design:

Post-hoc AKIKI & AKIKI-2 • Weaning attempt = ≥ 72 h without RRT • Success = no RRT restart within 7 days



The UNDERSCORE model (6 items)

- RRT duration
- Septic shock at admission
- Baseline creatinine
- Urine output (Day 4)
- Vasopressors (Day 4)
- Mechanical ventilation (Day 4)

Performance

- AUC 0.86 (derivation)
- AUC 0.73 (external validation)

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Keywords: Acute kidney injury, Renal replacement therapy, Weaning score

Introduction

Acute kidney injury (AKI) is common among intensive care unit (ICU) patients and is associated with high morbidity and mortality [1]. Renal replacement therapy (RRT) is a cornerstone in the management of such patients [2]. Although the safety of RRT has improved over time, the technique is still associated with complications, including bleeding, hemodynamic instability, catheter-related infections, thrombosis, and delayed renal recovery [3, 4].

Determining the optimal timing for both initiation and discontinuation of RRT remains a daily challenge for intensivists. Over the past decade, the question of when to initiate RRT has been clarified. Three large randomized controlled trials, AKIKI, IDEAL-ICU, and STARRT-AKI, have shown that, in the absence of immediate life-threatening complications, RRT initiation can safely be delayed, allowing 38 to 49% of patients with severe AKI to avoid RRT [5–8]. This conservative approach, also known as the delayed or watchful waiting RRT strategy, is now considered as the standard of care [2, 7, 9].

Take-home message

A simple six-item score (UNDERSCORE) calculated after a clinician-initiated RRT weaning attempt predicts successful weaning from RRT in ICU patients with severe AKI managed with a conservative strategy. In an external cohort with a different case-mix, the score maintained acceptable discrimination, supporting its use to inform post-discontinuation decisions such as whether to maintain access for potential restart or consider catheter removal.

By contrast, guidance on the optimal timing of RRT discontinuation is sparse, despite growing recognition of its clinical importance. Prolonged RRT is associated with delayed renal function recovery and increased health-care costs [4]. The lack of robust, evidence-based criteria to guide RRT discontinuation has been explicitly highlighted in the KDIGO guidelines [10], leaving substantial room for clinician judgement when deciding whether RRT can be stopped. Current expert research agendas mainly highlight the need for structured parameters to support decisions related to stopping RRT [11], yet they do not specify how clinicians should evaluate the likelihood of success once a discontinuation attempt has been made. In daily practice, this leaves clinicians without

objective tools to anticipate the likelihood of success once a weaning attempt has been initiated.

Earlier studies of RRT weaning prediction included patients who might not have required RRT in the first place, limiting the relevance of their findings in the current era. This justifies a renewed investigation of this issue, in light of modern RRT practices.

In the present study, we aimed to identify clinical predictors of successful RRT discontinuation in a homogeneous population of ICU patients who received RRT according to a conservative initiation approach. We specifically focused on a later time point for assessing weaning potential, an approach that has been rarely studied. Based on clinician-led discontinuation attempts, our objective was to develop and validate a prognostic model estimating the probability of sustained RRT discontinuation. We then externally validated the model in a separate ICU cohort.

Methods

Design and patients

This study is a *post-hoc* analysis of merged data from two multicentre randomized controlled trials evaluating RRT initiation strategies in critically ill patients: AKIKI (Artificial Kidney Initiation for Kidney Injury) and AKIKI-2.

The AKIKI trial was conducted in 31 ICUs in France between September 2013 and January 2016 and

compared early versus delayed RRT initiation in critically ill patients with severe AKI, defined by KDIGO stage 3 criteria. The AKIKI-2 study was conducted in 39 ICUs in France from May 2018 to December 2019 and included a similar patient population in an observational phase where all patients were managed using the same delayed RRT initiation strategy as in AKIKI. Patients who met one or both of the following criteria, blood urea nitrogen (BUN) level higher than 112 mg per deciliter and/or oligo-anuria for more than 72 h, were subsequently randomized to either a standard delayed strategy or an even more delayed initiation strategy.

Both trials received ethical approval by the competent French legal authority (Comité de Protection des Personnes d'Ile de France VI for AKIKI and Comité de Protection des Personnes de Sud-Est V for AKIKI-2).

For the present study, we screened all adult patients with KDIGO stage 3 AKI who received RRT according to a delayed initiation strategy (now better known as the conservative initiation approach). The patients included were those from the delayed arm in AKIKI and from the control arm of AKIKI2 (managed under the same delayed-initiation strategy as AKIKI). They were receiving or had received invasive mechanical ventilation and/or vasopressor therapy. Patients were eligible for inclusion in this study if they had undergone an attempt to discontinue RRT, defined as cessation of RRT, regardless

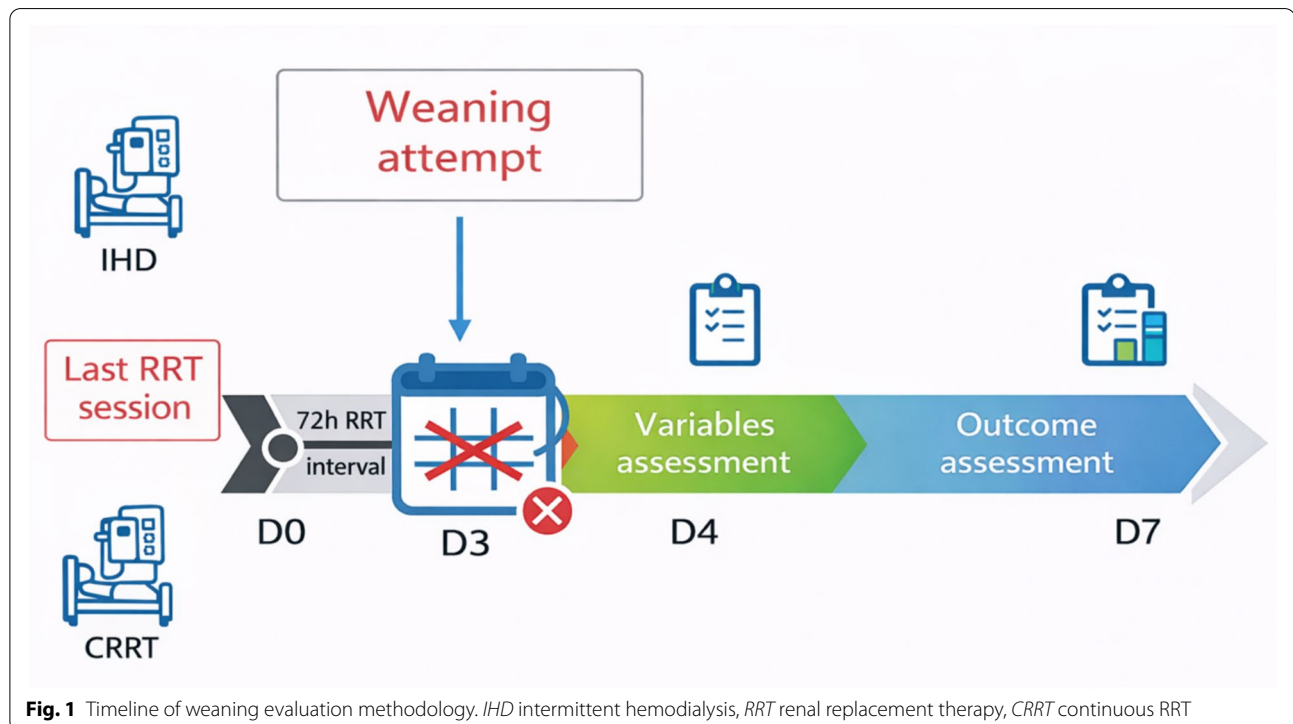


Fig. 1 Timeline of weaning evaluation methodology. IHD intermittent hemodialysis, RRT renal replacement therapy, CRRT continuous RRT

of modality (intermittent hemodialysis or continuous RRT), for at least three consecutive days.

In the original trials, the clinician's explicit decision to wean RRT was not systematically recorded. For the purposes of this study, we therefore used an operational definition of a weaning attempt based on the actual RRT schedule. A weaning attempt was defined a posteriori as any interruption of RRT, regardless of modality, lasting at least 72 consecutive hours. This data-driven definition was chosen to approximate a true clinician-intended discontinuation and to distinguish weaning attempts from the usual spacing of intermittent sessions or short, procedure-related interruptions (e.g., for surgery or transport to imaging such as CT scan) of continuous techniques. Day 0 (D0) was defined as the calendar day of the last RRT session preceding the start of this RRT free interval (Fig. 1).

Outcome

The primary outcome was the successful discontinuation of RRT, defined as being alive and free of any new RRT session within 7 days following the last RRT session.

Data collection and timeline

In both AKIKI and AKIKI2, clinical and biological data were collected daily from study inclusion until day-28 of ICU stay.

We collected baseline variables, including demographic characteristics, comorbidities, reason for ICU admission, severity scores at ICU admission, septic shock on admission, baseline serum creatinine, and the presumed causes of AKI. Baseline serum creatinine was defined as the patient's stable pre-hospital value, measured within the 12 months preceding ICU admission; when unavailable, it was back-calculated using the MDRD equation, in accordance with the original AKIKI and AKIKI2 protocols. In addition, we extracted clinical and laboratory data on day 4 (D4), defined as the first calendar day following completion of the 72-h RRT-free interval, which also corresponds to the day that would have followed the next scheduled RRT session if no weaning attempt had occurred (Fig. 1).

Urinary urea and urinary creatinine concentrations were not included in the current study due to a high proportion of missing data. These parameters were not systematically collected in the original trials, reflecting routine ICU practice, where daily urinary biochemistry is not consistently performed.

Statistical analysis

Patients were divided into two groups based on the primary outcome: the "weaning success" and "weaning failure".

Quantitative variables were described using mean $\pm$ SD, while qualitative variables were expressed as counts and percentages.

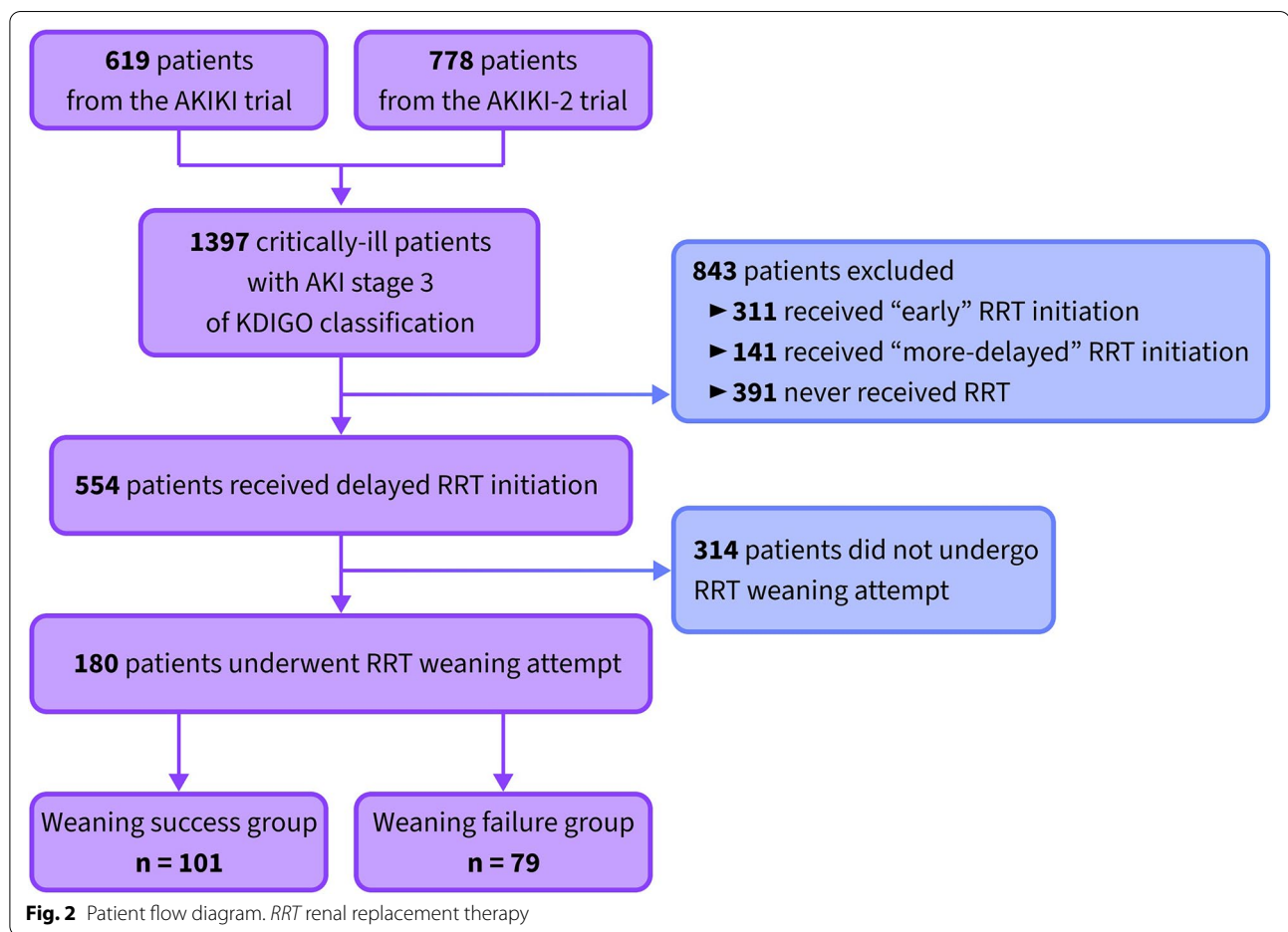
Univariate statistical analyses were performed to compare the weaning success and weaning failure groups, after verifying assumptions of validity. Student's *t*-test was used for continuous variables, and Chi-square or Fisher's exact test were applied for categorical variables, as appropriate.

A multivariable logistic regression model was fitted to identify independent predictors of successful RRT discontinuation (Supplementary Appendix Table S1, S2). Variable selection was based on both clinical relevance and statistical significance in univariate analyses ($p < 0.05$). To enhance bedside applicability, a simplified score, called the UNDERSCORE (for UNplugging a Dialysis catheter in the context of an Endgame RRT process SCORE, where "endgame" denotes the final phase of the RRT course after a clinician-initiated discontinuation attempt), was developed. The weight assigned to each predictor in the score was derived from its odds ratio in the multivariable model.

Predictor weights were derived from the multivariable model (based on effect size), and regression coefficients were rounded to the nearest whole integer. Selected continuous predictors (e.g., urine output, duration of RRT, baseline serum creatinine) were dichotomized using optimal cut-offs defined by the Youden index (maximizing sensitivity + specificity - 1, i.e., Youden's J).

Discrimination of the score was assessed using the area under the receiver operating characteristic (ROC) curve (AUC). An optimal threshold was chosen to balance sensitivity and specificity. This threshold was then used to classify patients as "suitable" or "not suitable" for RRT discontinuation, and performance at this cut-off was summarized in a confusion matrix (Supplementary Appendix).

Internal validation was performed using bootstrap resampling ($B = 2000$). For each replicate, a bootstrap sample of the derivation cohort (sampled with replacement and of the same size as the original dataset) was drawn. Model updating consisted of refitting the recalibration model linking the score to the outcome within the bootstrap sample. Discrimination (AUC) and threshold-based classification performance (sensitivity, specificity, PPV and NPV for score ≥ 2) were computed in the bootstrap sample, and the recalibration model fitted in the bootstrap sample was then applied to the original dataset to obtain test performance. Optimism was defined for each metric as the difference between bootstrap (apparent) performance and performance when evaluated on the original data using the bootstrap-fitted recalibration, and the mean optimism across replicates was subtracted



from the apparent estimates to yield optimism-corrected performance. Percentile 95% confidence intervals were derived from the bootstrap distributions.

Candidate models and selection

As shown in Table S1, we started from the set of variables available at baseline (ICU admission) and from day 3 to day 4 after the last RRT session, and we first screened their univariable associations with weaning success. We then built a limited number of prespecified candidate specifications, explicitly reported in Table S3, rather than using an automated stepwise selection procedure. Model 1 deliberately included the full set of candidate variables listed in Table S1, whereas Model 2 explored a more “dynamic” representation by adding pH at day 4 and trajectory-type variables and repeated creatinine measures (days 3 and 4). Model 3 retained only the predictors that remained significant in multivariable analysis (as detailed in Table S2): RRT duration before the attempt, urine output at day 4, vasopressor use at day 4, septic shock at ICU admission, and mechanical ventilation at day 4. Finally, Model 4 corresponded to a prespecified

updating-by-extension strategy. In the external cohort, an updating subset was used to screen a predefined list of clinically plausible candidate predictors not included in the original model and to select one additional predictor for inclusion based on its univariable association with weaning success and clinical coherence. The extended model specification was then refitted exclusively in the derivation cohort, with all regression coefficients re-estimated, and the updated model was locked prior to external testing in an independent hold-out subset.

Missing values were assumed to be missing at random. For each derivation dataset, missing data were handled using multiple imputation. For variables with informative missingness, an imputation by failure approach was applied.

In the Swiss cohort, we used non-parametric single imputation with the missForest algorithm, which iteratively trains random forests to predict missing entries. All candidate predictors were included in the imputation model, and the outcome was excluded. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC), with 95%

Table 1 Baseline patients characteristics^a

Characteristic	All n = 180	Weaning failure group n = 79	Weaning success group n = 101	p value
Age—years	63 ± 13	63 ± 13	63 ± 13	–
Sex—no. (%)				0.56
Male	127 (71)	54 (68)	73 (72)	
Female	63 (29)	25 (32)	28 (28)	
Serum creatinine before ICU admission ^b	1.02 ± 0.33	1.02 ± 0.28	1.02 ± 0.35	–
Coexisting conditions—no. (%)				
Chronic kidney disease ^c	24 (13)	10 (13)	14 (14)	0.81
Congestive heart failure	13 (7)	6 (8)	7 (7)	0.86
Hypertension	96 (53)	36 (46)	60 (60)	0.06
Diabetes mellitus	45 (25)	18 (23)	27 (27)	0.54
Ischemic heart disease	20 (11)	5 (6)	15 (14)	0.07
SAPS III at enrollment	72 ± 17	74 ± 18	71 ± 17	0.39
Septic shock ^g	104 (58)	54 (68)	50 (49)	0.01
Physiological support				
Invasive mechanical ventilation	159 (88)	70 (89)	89 (88)	0.81
Vasopressor support (epinephrine or norepinephrine)	136 (76)	59 (75)	77 (76)	
Cause of AKI—no./total no. (%)				
Shock	141 (78)	60 (75)	81 (80)	0.49
Sepsis	130 (72)	59 (75)	71 (70)	0.51
Rhabdomyolysis	15 (8)	5 (6)	10 (9)	0.38
Nephrotoxic agent	70 (39)	35 (44)	35 (35)	0.19

Bold indicates statistically significant differences

^a Plus-minus values are means ± SD. To convert values for creatinine to micromoles per liter, multiply by 88.4

^b The serum creatinine concentration before ICU admission was either determined with the use of values measured in the 12 months preceding the ICU stay or was estimated

^c Kidney function was reassessed with Cockcroft formula using available serum creatinine at baseline

^d The Simplified Acute Physiology Score (SAPS) III ranges from 0 to 146, with higher scores indicating more severe disease and a higher risk of death

^e The Sepsis-related Organ Failure Assessment (SOFA) score ranges from 0 to 24, with higher scores indicating more severe organ failure

^f Some patients were exposed to more than one nephrotoxic agent

^g Septic shock was defined as sepsis-induced hypotension despite fluid resuscitation of at least 30 ml per kilogram of body weight of intravenous fluid administered within the period spanning the 4 h before and 4 h after initiation of vasopressor therapy

confidence intervals computed using DeLong's method. Calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test.

All analyses were performed using R version 4.2.0.

External validation

To assess the external validity of the score, we used an independent ICU cohort from the Geneva University Hospitals (Switzerland). This cohort consisted of consecutive adult patients admitted between January 2010 and March 2025 who received RRT for AKI. Data were retrospectively collected from electronic health records and extracted in a structured format.

Patients were included if they had undergone a weaning attempt, defined as at least 72 consecutive hours without RRT, and were excluded if they had a history of chronic kidney disease requiring maintenance dialysis, consistent with the derivation cohort. Weaning success was defined

as the absence of any RRT session within seven days following cessation.

The study protocol was reviewed and approved by the Cantonal Commission for Research Ethics (CCER), Geneva, Switzerland, under reference number 2025-00851.

Results

Patients and outcomes

Among the 554 patients from the AKIKI and AKIKI2 studies who received RRT under a delayed-initiation strategy, a weaning attempt was performed in 180 patients, who were included in the primary analysis (Fig. 2). Overall, 101 patients (56%) achieved successful discontinuation of RRT. Among the 79 weaning failures, 29 patients died before day 7; 11 of these deaths followed withdrawal of life-sustaining therapy (WLST). Three additional patients underwent WLST but survived.

Items	Points
RRT time exposure until weaning attempt > 8 days	-1
Vasopressor agent the day after the weaning attempt	-1
Septic shock on admission	-1
Baseline serum creatinine > 116 μ mol/L	-1
Mechanical ventilation the day after the weaning attempt	+2
Urine output the day after the weaning attempt > 1 300 ml/d	+3

- **UNDERScore ≥ 2 :** High probability of weaning success; consider RRT catheter removal
- **UNDERScore < 2:** High probability of weaning failure; consider RRT reinitiation

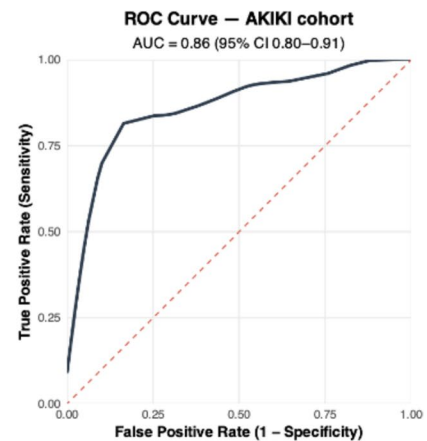


Fig. 3 The UNDERScore* for predicting successful weaning of RRT in ICU. Urine output corresponds to total 24-h urine volume the day after the weaning attempt (D4), with or without diuretics. *UNplugging a Dialysis catheter in the context of an Endgame RRT process SCORE. RRT: renal replacement therapy

Baseline characteristics are summarized in Table 1. Shock and sepsis were the most frequent causes of AKI.

Factors associated with successful RRT weaning

There were no meaningful differences between the weaning success and weaning failure groups in age, comorbidities (chronic kidney disease, congestive heart failure, hypertension, diabetes mellitus), or baseline severity scores (SAPS and SOFA). Septic shock on ICU admission was more frequent among weaning failures than among weaning successes (68% vs 49%, $p=0.01$).

In univariable analyses, successful weaning was associated with a shorter RRT duration before the attempt, lower serum creatinine on days 3 and 4, higher urine output on day 4, less frequent vasopressor use on day 4, and mechanical ventilation status on day 4 (Table S1).

In multivariable logistic regression, five variables were independently associated with successful weaning: urine output on day 4, duration of RRT before the weaning attempt, vasopressor use on day 4, invasive mechanical ventilation on day 4, and septic shock at ICU admission.

External cohort and model extension with independent test-set validation

To improve the transportability of the score beyond the original trial setting, we deliberately sought a markedly different external population and practice environment. We therefore used an external cohort from the ICU of the Geneva University Hospitals (Switzerland), spanning 2010–2025, where RRT initiation was not protocolized and left to the treating physician. The case mix was

intentionally broader than in the derivation cohort, notably including cardiac and neurosurgical patients and liver transplant recipients.

During the study period, 878 adult ICU patients received RRT. Among them, 415 (47%) underwent a weaning attempt as defined in the Methods, and 338 (81%) achieved successful weaning. Compared with the derivation cohort, the external cohort differed substantially in baseline characteristics and admission diagnoses, including a lower proportion of septic shock (93 patients, 22%), reflecting a wider spectrum of clinical profiles.

Following a descriptive assessment of performance in the full Swiss cohort (C2), we conducted the prespecified updating procedure using a random split into C2-update ($n=124$, 30%) and C2-test ($n=291$, 70%). The extension step retained baseline serum creatinine as the additional predictor, yielding Model 4.

Score derivation and model performance

In the derivation cohort, the continuous-predictor model yielded an AUC of 0.86 (95% CI 0.80–0.91) (Fig. 3a). Calibration was satisfactory, with a null calibration-in-the-large (0.00; 95% CI -0.37 – 0.37), a calibration slope close to unity (slope=1.00; 95% CI 0.72–1.28) (Fig. 3, Figure S2), and good agreement between predicted and observed risks (Hosmer–Lemeshow $p=0.293$). Overall accuracy was good, with a Brier score of 0.15 (95% CI 0.12–0.18).

To facilitate bedside use, the UNDERScore was derived from the updated model (Model 4) by rounding regression coefficients to integer points and dichotomizing continuous predictors using clinically usable cutoffs:

urine output $>1,300$ mL/day, RRT duration ≤ 8 days, and baseline serum creatinine >116 $\mu\text{mol/L}$ (≈ 1.31 mg/dL). The decision threshold was initially estimated at 1.6 points and rounded to 2 points.

After dichotomization (including the baseline creatinine threshold), discrimination remained unchanged with an AUC 0.86 (95% CI 0.80–0.91). Using the 2-point threshold, sensitivity was 73% (95% CI 64–82), specificity 90% (95% CI 81–96), PPV 90% (95% CI 82–96), and NPV 72% (95% CI 63–81).

Internal validation

Bootstrap internal validation (2000 resamples) confirmed the robustness of the score. The AUC remained stable with an apparent AUC of 0.86, and a bootstrap 95% CI of 0.80–0.91 (optimism-corrected AUC 0.86). Overall accuracy remained good, with a Brier score of 0.15 (bootstrap 95% CI 0.12–0.18; optimism-corrected 0.16).

External test-set performance

Final external performance was evaluated only in the Swiss test set (C2-test). Discrimination was moderate, with an AUC of 0.73 (95% CI 0.66–0.80). Using the 2-point threshold, sensitivity was 76% (95% CI 71–80), specificity 55% (95% CI 43–66), PPV 88% (95% CI 84–92), and NPV 34% (95% CI 26–43).

Discussion

The DOORS study aimed to develop and validate the UNDERSCORE, a simple and clinically applicable bedside tool to guide decisions regarding RRT discontinuation in critically ill patients with severe AKI. The score was derived from a multivariable model built on the derivation cohort, which identified urine output, invasive mechanical ventilation and vasopressor support after the weaning attempt, duration of RRT prior to the attempt, and presence of septic shock on admission as significant predictors of weaning success. Baseline serum creatinine was also included in the final version of the score to reflect its clinical relevance and the results observed during external validation. The UNDERSCORE demonstrated strong predictive performance in the derivation cohort and fair performance in an independent external cohort.

Previous studies exploring criteria for successful RRT weaning were conducted before the endorsement of a delayed RRT initiation strategy for severe AKI [9]. Most studies included in a 2020 meta-analysis on RRT discontinuation [12] predate the publication of the large randomized controlled trials (AKIKI, IDEAL-ICU,

STARTRT-AKI) on RRT initiation [5–8]. Consequently, earlier cohorts may have included patients that would not have required RRT under current standards, thereby confounding the discourse on RRT discontinuation timing [13].

Furthermore, studies addressing RRT discontinuation have evaluated weaning success at highly variable time points, from during ongoing RRT to immediately at cessation or shortly thereafter, reflecting the absence of a consensual framework regarding when recovery should be assessed. In routine practice, however, attempting RRT discontinuation is usual care and rarely carries major immediate harm, as treatment can generally be resumed if needed. Thus, the key clinical question is not whether to attempt discontinuation, but what is likely to happen after it. This contrasts with mechanical ventilation, where premature weaning can lead to acute respiratory failure, emergency reintubation, and increased mortality, justifying tools to determine when ventilator weaning attempt should be initiated. Because RRT can usually be restarted without a major immediate harm, directly transposing mechanical ventilation weaning paradigms to RRT discontinuation seems conceptually inappropriate. On this basis, the DOORS study focused on clinician-initiated discontinuation attempts and collected variables after a 72 h RRT free interval, chosen to distinguish true discontinuation from routine session spacing, on the day following the next expected session (i.e. D4), to estimate the risk of subsequent reinitiation. In line with this pragmatic perspective, successful discontinuation was defined as being alive and free of any RRT resumption within 7 days, reflecting the clinically meaningful goal of remaining dialysis-free after a discontinuation attempt.

At this time point, several clinical factors emerged as strong predictors of weaning success, many of which are consistent with prior literature. Variables such as urine output and RRT duration have repeatedly been identified as key indicators of renal recovery [14–16]. Urine output was retained in the score with a threshold of 1300 mL/24 h. This cut-off was derived in a data-driven manner in the derivation cohort using a post-discontinuation assessment at day 4. Since urine output was measured after additional time to recover urine output after stopping RRT, this value is not directly comparable with cut-offs reported in other studies that assessed urine output at the time of RRT cessation or during ongoing RRT, and may therefore appear higher than some previously published values [12]. The associations between septic shock on admission and vasopressor use with weaning failure also align with existing evidence that greater illness severity is negatively associated with renal recovery [12]. Chronic kidney disease (a factor closely related to baseline creatinine) has also previously been linked to a

reduced likelihood of successful RRT discontinuation. A recent meta-analysis reported a pooled odds ratio of 0.638 (95% CI 0.491–0.829) for CKD as a negative predictor of short-term RRT liberation [17].

Interestingly, the need for invasive mechanical ventilation on the day following RRT discontinuation was positively associated with weaning success, an unexpected finding, as invasive mechanical ventilation is typically considered a marker of greater illness severity and has been associated with impaired renal recovery. One possible explanation is that clinicians may perceive the risk of acute respiratory decompensation due to fluid overload as more critical in spontaneously breathing patients. In contrast, for intubated patients, this risk is mitigated by ventilatory support, which may make clinicians more comfortable with withholding RRT. This finding should therefore not be interpreted as a causal benefit of mechanical ventilation on renal recovery. Rather, it likely reflects differences in how volume status and its respiratory consequences are perceived and weighted in clinical decision-making after a discontinuation attempt.

Our study has several strengths. First, the derivation cohort was homogeneous and well-defined, including only patients managed according to a conservative RRT initiation approach for severe AKI [2, 9]. Then, the DOORS study is the first to evaluate RRT discontinuation predictors in a population of patients with homogeneous RRT initiation criteria, which selected patients who really needed RRT initiation. Second, we focused on a clinically meaningful time point, the day after the weaning attempt, and selected only readily available bedside variables, making the UNDERSCORE a pragmatic and easy-to-implement tool. This approach provides new insight into a frequently encountered but poorly standardized clinical decision: when it is safe and appropriate to remove the RRT catheter. By concentrating on this specific juncture and leveraging practical, objective parameters, we offer novel and actionable guidance to intensivists. Third, we deliberately validated UNDERSCORE in an external cohort with a markedly different case mix, including patients from cardiac surgery, liver transplantation, and neurosurgery, and with more heterogeneous RRT initiation protocols. Despite these differences, the UNDERSCORE maintained acceptable discrimination (AUC 0.73) supporting its potential generalizability across diverse ICU populations. This lower performance compared with the derivation cohort may also partly reflect the contrast between highly selected trial populations and unselected patients treated in routine care, whose characteristics and management may differ from those of trial participants.

The primary limitation of the DOORS study lies in its specific focus on ICU patients with multi-organ failure. Consequently, our findings may not be generalizable to patients with isolated AKI or those with different underlying conditions, such as rapidly progressive glomerulonephritis and other renal manifestations of systemic diseases. However, the external validation cohort did include a broader case mix, notably patients without shock, which supports a degree of applicability beyond the original population. Finally, this study is based on post hoc analyses of previously conducted trials and observational data and should be considered exploratory, as the intentionality of an RRT-free interval cannot always be formally established; accordingly, the proposed score threshold (Fig. 3) should not be interpreted as a stand-alone decision rule and requires prospective validation before being used to guide clinical management. The definition of a weaning attempt as three consecutive days without RRT should likewise be interpreted as a pragmatic, albeit inherently arbitrary, threshold.

In summary, the DOORS study addresses a critical knowledge gap by providing a structured framework to support decisions around when to stop RRT in critically ill patients. The UNDERSCORE tool offers a practical, bedside-ready resource to assist clinicians in optimizing the management of severe AKI, with the potential to improve both patient outcomes and resource utilization.

Supplementary Information

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Author contributions

All authors contributed substantially to this work and approved the final version for submission. Concept and design: KC, SG, YA, DD, DL. Data curation:

AKIKI/AKIKI2 steering groups and site investigators; Geneva ICU team; KC, YA, DL. Statistical analysis and modelling: KC, YA, FS, DL. Interpretation of data: all authors. Drafting of the manuscript: all authors. Critical revision for important intellectual content: all authors.

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Data availability

De-identified data from AKIKI and AKIKI2 are available upon reasonable request and subject to approval by the respective steering committees and data-sharing agreements. Access to the Geneva ICU external-validation dataset requires permission from the local data custodian. Requests should be addressed to the corresponding author, who will coordinate with the relevant committees.

Declarations

Conflicts of interest

The authors declare no competing interests.

Ethics approval

The AKIKI trial was approved by the Comité de Protection des Personnes Île-de-France VI; AKIKI2 was approved by the Comité de Protection des Personnes Sud-Est V for all participating French centers. The DOORS analysis used de-identified data from these trials. The external-validation cohort obtained approval from the local ethics committee in Geneva, with waiver of informed consent owing to the retrospective analysis of de-identified data, in accordance with local regulations.

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